

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
21 May 2004 (21.05.2004)

PCT

(10) International Publication Number
WO 2004/041067 A3

(51) International Patent Classification:
A01N 37/18 (2006.01) C07K 5/00 (2006.01)
A61K 38/00 (2006.01) C07K 14/00 (2006.01)
C07K 2/00 (2006.01) C07K 17/00 (2006.01)
C07K 4/00 (2006.01)

(74) Agent: CELLI, Rosemarie; Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111-3834 (US).

(21) International Application Number:
PCT/US2003/034527

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 31 October 2003 (31.10.2003)

(84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(25) Filing Language: English

Published:

— with international search report

(26) Publication Language: English

(88) Date of publication of the international search report:
28 December 2006

(30) Priority Data:
60/423,012 1 November 2002 (01.11.2002) US

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(71) Applicants: ELAN PHARMACEUTICALS, INC. [US/US]; 800 Gateway Boulevard, South San Francisco, CA 94080 (US). THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 1111 Franklin Street, 5th Floor, Oakland, CA 94607 (US).

(72) Inventors: SCHENK, Dale, B.; 1542 Los Altos Drive, Burlingame, CA 94010 (US). MASLIAH, Eliezer; 4661 Corte Mar Corazon, San Diego, CA 92130 (US).



WO 2004/041067 A3

(54) Title: PREVENTION AND TREATMENT OF SYNUCLEINOPATHIC DISEASE

(57) Abstract: The invention provides improved agents and methods for treatment of diseases associated with synucleinopathic diseases, including Lewy bodies of alpha-synuclein in the brain of a patient. Such methods entail administering agents that induce a beneficial immunogenic response against the Lewy body. The methods are particularly useful for prophylactic and therapeutic treatment of Parkinson's disease.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/34527

A. CLASSIFICATION OF SUBJECT MATTER

IPC: A01N 37/18(2007.01);A61K 38/00(2007.01);C07K 2/00(2007.01),4/00(2007.01),5/00(2007.01),14/00(2007.01),17/00(2007.01)

USPC: 530/300,350;514/2;424/184.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 530/300, 350; 514/2; 424/184.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIPPA et al. Antibodies to alpha-synuclein detect Lewy bodies in many Down's syndrome brains with Alzheimer's disease. Ann. Neurol. March 1999, Vol 45, No. 3, pages 353-357.	57, 59, 71-72
X	WAKABAYASHI K. NACP, a presynaptic protein, immunoreactivity in Lewy bodies in Parkinson's disease. Neurosci. Lett. December 1997, Vol 239, No. 1, pages 45-48.	57, 59, 71-72
X	IRIZARRY M.C. Nigral and cortical Lewy bodies and dystrophic nigral neurites in Parkinson's disease and cortical Lewy body disease contain alpha-synuclein immunoreactivity. J. Neuropathol. Exp. Neurol. April 1998, Vol 57, No. 4, pages 334-37.	57, 59, 71-72
X	WAKABAYASHI K. Alpha-synuclein immunoreactivity in glial cytoplasmic inclusions in multiple system atrophy. Neurosci. Lett. 1998, Vol 249, pages 180-182.	57, 59, 71-72
A	WO99/40191 A1 (DNAS OR GENES PARTICIPATING IN PARKINSON'S DISEASE) 12 August 1999 (12.08.1999), Abstract only (Japanese language document).	1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72

<input checked="" type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
*	Special categories of cited documents	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Z"	document number of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date cited		
Date of the actual completion of the international search		Date of mailing of the international search report	
16 August 2006 (16.08.2006)		02 OCT 2006	
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner of Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 273-3201		Authorized officer Janet Andres Telephone No 571-272-1600	

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	US 2002/0151464 A1 (WOLOZIN et al) 17 October 2002 (17.10.2002), full document, particularly Example 9.	1, 3, 8-10, 13-14, 36-41, 45-57, 59, 62, 71-72
X — Y	WO00/72876 A2 (NEURALAB LIMITED.) 07 December 2000 (07.12.2000), full document, particularly p. 114 and claims.	1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72
X — Y	WO99/27944 A1 (ATHENA NEUROSCIENCES, INC.) 10 June 1999 (10.06.1999), see full document.	1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72
X — Y	US 6,504,080 B1 (VAN DER PUTTEN P.H.) 07 January 2003 (07.01.2003), see full document.	1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72
		1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/34527

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1,3,8-11,13,14,36-41,45-57,59,62,71 and 72

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/34527

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72 in part drawn to a method of preventing or treating via technical feature alpha-synuclein.

Group II, claim(s) 1, 2, 17-29, 33-41, 45-56, 57-58, 62, 71-72 in part drawn to a method of preventing or treating via technical feature antibodies to alpha-synuclein.

Group III, claim(s) 1, 4, 8-10, 12, 15, 16, 36-41, 45-56, 57, 59, 60, 62, 71-72 in part drawn to a method of preventing or treating via technical feature immunogenic fragment of alpha-synuclein.

Group IV, claims 1, 4-5, 8-10, 12, 15, 16, 36-41, 45-56, 57, 59, 60, 62, 71-72 in part drawn to a method of preventing or treating via technical feature amino acids 35-65 of alpha synuclein.

Group V, claim(s) 1, 4, 6, 8-10, 12, 15, 16, 36-41, 45-56, 57, 59-60, 62, 71-72 in part drawn to a method of preventing or treating via technical feature alpha-synuclein fragment comprising amino acids 130-140.

Group VI, claim(s) 1, 4, 7-10, 12, 15-16, 36-41, 45-57, 59-60, 62, 71-72 in part drawn to a method of preventing or treating via technical feature alpha-synuclein C-terminal fragment.

Group VII, claim(s) 1, 8-10, 17-29, 30-41, 45-56 in part drawn to a method of preventing or treating via technical feature polynucleotide encoding antibody.

Group VIII, claim(s) 42-43, 45-56, 57, 62, 71-72 in part drawn to a method of preventing or treating via technical feature Abeta peptide or fragment.

Group IX, claim(s) 42, 44 45-56, 57, 58, 62, 71-72 in part drawn to a method of preventing or treating via technical feature antibodies to Abeta or antibody fragment.

Group X, claim(s) 57, 59, 62 in part drawn to a pharmaceutical composition to the extent of 6CHC-1 or immunogenic fragment.

Group XI, claim(s) 57, 59, 60-62, drawn in part to a pharmaceutical composition to the extent of NAC.

Group XII, claim(s) 65 drawn to a method of screening an antibody via contact with neuronal cell.

Group XI, claim(s) 66 drawn to a method of screening and antibody via determining specific binding with peptide of at least five amino acids of alpha synuclein.

Group XII, claim(s) 67-70 drawn to a method of screening and agent via contacting with a transgenic.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of claim 1, alpha synuclein is anticipated by prior art, see in particular Jensen et al., Biochem J., 1997 Apr 15;323 (Pt 2):539-46 which teaches technical features alpha-synuclein, beta-synuclein, NAC and Abeta as well as binding thereto. Thus the technical features are not a contribution over the prior art and unity is therefore lacking. Further, the subsequent inventions are each separable as they recite different technical feature agents that differ in structure and function. The methods are similarly separable as they are comprised of different

INTERNATIONAL SEARCH REPORT

PCT/US03/34527

technical feature reagents, steps, functions, outcomes and effects. Accordingly, the inventions are separable and lack unity. Claims 63-64 are not included as the claims are improperly multiple dependent claims.